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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,504	08/21/2001	Toshio Ota	084335/0133	2313

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,504	OTA ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,12-14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,12-14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed July 1, 2003. Currently, claims 1-19 are pending. Claims 7-9, 11, 15, 17-19 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

Priority

4. This application claims priority to PCT/JP99/04549, filed August 24, 1999. The application also claims priority to Japanese foreign document 10/262941, filed September 17, 1998.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The certified translation filed July 1, 2003 has been placed in the file.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-6, 10, 12-14, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (US Pat. 5,837,468, November 17, 1998) in view of Dynal Catalog (Biomagnetic Techniques in Molecular Biology, pages 43-50, 1998).

It is noted that Claims 10, 12-14, 16 are directed to Product-by-Process Claims.

> As provided in the MPEP 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Wang et al. (herein referred to as Wang) teaches a method of generating PCR-based cDNA libraries with anchored ends and isolating the ends of a cDNA clone. As seen in Figure 1, a simple PCR based method for generating a cDNA library with anchored ends is presented. The mRNA is reverse transcribed using a polyTV primer and Rtase to generate a first strand of cDNA. The cDNA is then dC-tailed and the cDNA is further amplified using a poly TV and Poly GH primer for amplification such that

a full length cDNA library is generated with anchored ends. A cDNA library is produced that contains full-length cDNAs, anchored at both ends by known sequences, "anchored-end cDNA library" (col. 7, lines 28-32). As seen in Figure 1, the library contains specific additional adaptor sequences 5' and 3' of the poly T and polG sequences. Wang teaches that the driver cDNA library may be tagged using biotin-dCTP such that the subtractive hybridization step may be performed.

Wang does not specifically teach capturing the full length cDNAs .

However, Dynal specifically teaches generating a reusable solid-phase cDNA library. Dynal teaches construction of immobilized cDNA libraries for multiple RT-PCR amplifications. Dynal teaches using Dynabeads to capture mRNA to synthesized first-strand cDNA. Dynal teaches that the advantages of using Dynabeads for immobilized cDNA libraries includes creating a covalently linked first-strand cDNA. The construction of a reusable solid-phase cDNA library allows multiple downstream amplification of specific transcripts. Dynal outlines several additional advantages for using Dynabeads (page 45). As seen in Figure 10, mRNA is used to generate a reusable solid-phase cDNA library and downstream amplification products. Dynal teaches capturing using a polyT primer.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Wang to specifically encompass capturing full length immobilized cDNA libraries using polyT or polyG primers as taught by Dynal. The ordinary artisan would have clearly recognized that solid phase cDNA libraries were advantageous to allow generation of a reusable solid-phase cDNA library. Dynal teaches numerous reasons a reusable solid-phase cDNA

library is desirable including convenient cDNA storage and availability for studies of gene expression, for example (page 45-46). The method of Wang teaches that the polyTV and polyGV is used for PCR amplification, therefore, the ordinary artisan would have been motivated to have immobilized the poly TV and polyGV primers to a solid support to enable creating a solid-phase cDNA library.

Response to Arguments

The response traverses the rejection. The response asserts the biotin-dCTP is not incorporated into the primer which occupies the 5' side of the cDNA, and the resulting PCR product has biotin-dCTP incorporated at sites other than the 5' side. First, the specification states that "the immobilization of the 5'side includes the immobilization not only at 5' terminal but also close to the 5'-terminal of a sense strand of cDNA (page 8, lines 16-17). The claims are not limited to a cDNA immobilized library with only cDNAs immobilized at the 5' side. Furthermore, 5' side may be broadly interpreted to mean any 5' position of the center of the cDNA. Thus, as seen in Figure 2, the biotin may occur throughout the cDNA and may be used to isolate the full length cDNA. Thus, as written, the claims do not exclude nor are they limited to capturing the cDNA at the 5' terminal nucleotide bonded to the substrate. The arguments that Wang's cDNA tagged with biotin-dCTP cannot be immobilized at the 5' side is not accurate, as any of the biotin molecules may be immobilized and captured, including sites at the 5' side of the cDNA.

Alternatively, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642

F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The arguments points to the alleged deficiencies of each of the references, but does not consider the combination as a whole, as set forth in the rejection above. The cDNA fragments each contain either poly C or poly G, thus, capturing full length immobilized cDNA libraries using polyT and polyG to generate a full length library would have been obvious at the time the invention was made for the reasons specifically set forth above. Whether Wang specifically teaches using the "anchor regions" as means for immobilization, in combination with the teachings of Dynal, the skilled artisan would have been motivated to have immobilized full length cDNAs of Wang using the methods of Dynal. Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

7. Claims 1-6, 10, 12-14, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al (US Pat. 5,962,272, October 1999) in view of Belyavsky et al (US Pat. 5,814,445, September 29, 1998) and further in view of Dynal Catalog (Biomagnetic Techniques in Molecular Biology, pages 43-50, 1998).

It is noted that Claims 10, 12-14, 16 are directed to Product-by-Process Claims.

> As provided in the MPEP 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Chenchik et al. (herein referred to as Chenchik) teaches a method of generating full-length cDNA libraries. As seen in Figure 3-1, full length RNA is used to generate a full first-strand cDNA. A 5' PCR primer is then used to generate the second strand of cDNA thereby generating full length cDNA nucleic acids. Chenchik teaches the method is simple and generates high quality, full-length cDNA from RNA (col. 2, lines 38-40). Chenchik acknowledges that cDNA clones obtained from the full-length cDNA library prepared according to the method contains the complete information for the primary structure of the protein (col. 4, lines 55-56). The full-length cDNA library may be used to produce the encoded proteins or map the transcriptional start sites (col. 15, lines 20-25).

Chenchik does not specifically teach capturing the full length cDNAs .

However, Belvavsky et al. (herein referred to as Belvavsky) teaches a method of identifying and cloning differentially expressed mRNAs which involves capturing the nucleic acids via a microbead. As seen in Figure 6, first chain of cDNA is synthesized from RNA, a biotinylated primer is used to synthesize a second chain of cDNA, and the cDNA fragments are immobilized at the 5' terminus of the sense strand of the cDNA. Belvavsky teaches that after one synthesizes the first chain with the aid of a set of random hexamer primers, synthesis of the second chain with the aid of primer 1 containing a biotin group at the 5' end, immobilizes the cDNAs in streptavidin microgranules (col. 6-7).

Additionally, Dynal specifically teaches generating a reusable solid-phase cDNA library. Dynal teaches construction of immobilized cDNA libraries for multiple RT-PCR amplifications. Dynal teaches using Dynabeads to capture mRNA to synthesized first-strand cDNA. Dynal teaches that the advantages of using Dynabeads for immobilized

cDNA libraries includes creating a covalently linked first-strand cDNA. The construction of a reusable solid-phase cDNA library allows multiple downstream amplification of specific transcripts. Dynal outlines several additional advantages for using Dynabeads (page 45). As seen in Figure 10, mRNA is used to generate a reusable solid-phase cDNA library and downstream amplification products.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Chenchik to specifically encompass capturing full length immobilized cDNA libraries using biotinylated primers as taught by Belyavsky for the purposes taught by Dynal. The ordinary artisan would have clearly recognized that solid phase cDNA libraries were advantageous to allow generation of a reusable solid-phase cDNA library. Dynal teaches numerous reasons a reusable solid-phase cDNA library is desirable including convenient cDNA storage and availability for studies of gene expression, for example (page 45-46). The method of Chenchik and Belyavsky teaches that a biotinylated primer is used for PCR amplification, therefore, the ordinary artisan would have been motivated to have immobilized the primers to a solid support to enable creating a solid-phase cDNA library for the benefits taught by Dynal.

Conclusion

8. No claims allowable over the art.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
September 24, 2003

JEHANNE SOUAYA
PATENT EXAMINER
Primary

Jehanne Souaya
9/24/03